

WE CLAIM:

1. A method for accelerating the rate of mucociliary clearance in a subject in need of such treatment comprising administering to the subject an effective mucociliary clearance stimulatory amount of a composition comprising a Kunitz-type serine protease inhibitor and a physiologically acceptable carrier.

2. The method according to claim 1, wherein the composition is administered to the lung airways.

3. The method according to claim 1, wherein said composition is administered directly by aerosolization.

4. The method according to claim 1, wherein said composition is administered directly as an aerosol suspension into the mammal's respiratory tract.

5. The method according to claim 4, wherein said aerosol suspension includes respirable particles ranging in size from about 1 to about 10 microns.

6. The method according to claim 4, wherein said aerosol suspension includes respirable particles ranging in size from about 1 to about 5 microns.

7. The method according to claim 4, wherein said aerosol suspension is delivered to said subject by a pressure driven nebulizer.

8. The method according to claim 4, wherein said aerosol suspension is delivered to said subject by an ultrasonic nebulizer.

9. The method according to claim 4, wherein said aerosol suspension is delivered to said subject by a non-toxic propellant.

10. The method according to claim 1, wherein said carrier is a member selected from the group consisting of a physiologically buffered solution, an isotonic saline, normal saline, and combinations thereof.

11. The method according to claim 1 wherein the Kunitz-type serine protease inhibitor is aprotinin.

12. The method according to claim 1, wherein the Kunitz-type serine protease inhibitor comprises the amino acid sequence:

MAQLCGL RRSRAFLALL GSLLLLSGVLA -1
ADRERSIHDF CLVSKVVGRC RASMPRWYN VTDGSCQLFV YGGCDGNSNN 50
YLTKEECLKK CATVTENATG DLATSRNAAD SSVPSAPRRQ DSEDHSSDMF 100
NYEEYCTANA VTGPCRASFP RWYFDVERNS CNNFIYGGCR GNKNSYRSEE 150
ACMLRCFRQQ ENPPLPLGSK VVVLAGLFVM VLILFLGASM VYLIRVARRN 200

QERALRTVWS SGDDKEQLVK NTYVL

225

(SEQ ID NO.: 49).

13. The method according to claim 1, wherein the Kunitz-type serine protease
5 inhibitor comprises the amino acid sequence:

AGSFLAWL GSLLLLSGVLA -1

ADRERSIHDF CLVSKVVGRC RASMPRWYN VTDGSCQLFV YGGCDGNSNN 50

YLTKEECLKK CATVTENATG DLATSRNAAD SSVPSAPRRQ DSEDHSSDMF 100

NYEEYCTANA VTGPCRASFP RWYFDVERNS CNNFIYGGCR GNKNSYRSEE 150

10 ACMLRCFRQQ ENPPLPLGSK VVVLGAVS 179

(SEQ ID NO.: 2),

MLR AEADGVSRLI GSLLLLSGVLA -1

ADRERSIHDF CLVSKVVGRC RASMPRWYN VTDGSCQLFV YGGCDGNSNN 50

15 YLTKEECLKK CATVTENATG DLATSRNAAD SSVPSAPRRQ DSEDHSSDMF 100

NYEEYCTANA VTGPCRASFP RWYFDVERNS CNNFIYGGCR GNKNSYRSEE 150

ACMLRCFRQQ ENPPLPLGSK VVVLAGLFVM VLILFLGASM VYLIRVARRN 200

QERALRTVWS SGDDKEQLVK NTYVL 225

(SEQ ID NO.: 45),

20

MAQLCGL RRSRAFLALL GSLLLLSGVLA -1

ADRERSIHDF CLVSKVVGRC RASMPRWYN VTDGSCQLFV YGGCDGNSNN 50

YLTKEECLKK CATVTENATG DLATSRNAAD SSVPSAPRRQ DSEDHSSDMF 100

NYEEYCTANA VTGPCRASFP RWYFDVERNS CNNFIYGGCR GNKNSYRSEE 150

25 ACMLRCFRQQ ENPPLPLGSK VVVLAGLFVM VLILFLGASM VYLIRVARRN 200

QERALRTVWS FGD 213

(SEQ ID NO.: 47),

ADRERSIHDF CLVSKVVGRC RASMPRWYN VTDGSCQLFV YGGCDGNSNN 50

30 YLTKEECLKK CATVTENATG DLATSRNAAD SSVPSAPRRQ DSEDHSSDMF 100

NYEEYCTANA VTGPCRASFP RWYFDVERNS CNNFIYGGCR GNKNSYRSEE 150

ACMLRCFRQQ ENPPLPLGSK VVVLAGLFVM VLILFLGASM VYLIRVARRN 200

QERALRTVWS SGDDKEQLVK NTYVL 225

(SEQ ID NO.: 70),

35

and

ADRERSIHDF CLVSKVVGRC RASMPRWWYN VTDGSCQLFV YGGCDGNSNN 50
YLTKEECLKK CATVTENATG DLATSRNAAD SSVPSAPRRQ DSEDHSSDMF 100
5 NYEEYCTANA VTGPCRASFP RWYFDVERNS CNNFIYGGCR GNKNSYRSEE 150
ACMLRCFRQQ ENPPLPLGSK VVVLAGLFVM VLILFLGASM VYLIRVARRN 200
QERALRTVWS FGD 213
(SEQ ID NO.: 71)

10

14. The method according to claim 1, wherein the Kunitz-type serine protease inhibitor comprises the amino acid sequence:

IHDF CLVSKVVGRC RASMPRWWYN VTDGSCQLFV YGGCDGNSNN 50
15 YLTKEECLKK CATV 64
(SEQ ID NO.: 4),

CLVSKVVGRC RASMPRWWYN VTDGSCQLFV YGGCDGNSNN 50
YLTKEECLKK C 61
20 (SEQ ID NO.: 5),

YEEYCTANA VTGPCRASFP RWYFDVERNS CNNFIYGGCR GNKNSYRSEE 150
ACMLRCFRQ 159
(SEQ ID NO.: 6),

25

CTANAVTGPC RASFPRWYFD VERNSCNNFI YGGCRGNKNS YRSEE 150
ACMLRC 156
(SEQ ID NO.: 7),

30 IHDF CLVSKVVGRC RASMPRWWYN VTDGSCQLFV YGGCDGNSNN 50
YLTKEECLKK CATVTENATG DLATSRNAAD SSVPSAPRRQ DSEDHSSDMF 75
NYEEYCTANA VTGPCRASFP RWYFDVERNS CNNFIYGGCR GNKNSYRSEE 125
ACMLRCFRQ 159
(SEQ ID NO.: 3),

35

CLVSKVVGRC RASMPRWWYN VTDGSCQLFV YGGCDGNSNN 50
 YLTKEECLKK CATVTENATG DLATSRNAAD SSVPSAPRRQ DSEDHSSDMF 100
 NYEEYCTANA VTGPCRASFP RWYFDVERNS CNNFIYGGCR GNKNSYRSEE 150
 ACMLRC 156

5 (SEQ ID NO.: 50),

ADRERSIHDF CLVSKVVGRC RASMPRWWYN VTDGSCQLFV YGGCDGNSNN 25
 YLTKEECLKK CATVTENATG DLATSRNAAD SSVPSAPRRQ DSEDHSSDMF 75
 NYEEYCTANA VTGPCRASFP RWYFDVERNS CNNFIYGGCR GNKNSYRSEE 125
 10 ACMLRCFRQQ ENPPLPLGSK VVVLGAVS 179

(SEQ ID NO.: 1),

and

15 ADRERSIHDF CLVSKVVGRC RASMPRWWYN VTDGSCQLFV YGGCDGNSNN 50
 YLTKEECLKK CATVTENATG DLATSRNAAD SSVPSAPRRQ DSEDHSSDMF 100
 NYEEYCTANA VTGPCRASFP RWYFDVERNS CNNFIYGGCR GNKNSYRSEE 150
 ACMLRCFRQQ ENPPLPLGSK 170

(SEQ ID NO.: 52).

15. The method according to claim 1, wherein the Kunitz-type serine protease inhibitor comprises the amino acid sequence:

ADRERSIHDF CLVSKVVGRC RASMPRWWYN VTDGSCQLFV YGGCDGNSNN 50
 25 YLTKEECLKK CATVTENATG DLATSRNAAD SSVPSAPRRQ DS 92

(SEQ ID NO.: 8).

16. The method according to claims 12, 13, 14 or 15, wherein the Kunitz-type serine protease inhibitor is glycosylated.

17. The method according to claims 12, 13, 14 or 15, wherein the Kunitz-type serine protease inhibitor contains at least one intra-chain cysteine-cysteine disulfide bond.

18. The method according to claims 12, 13, 14, or 15, wherein the Kunitz-type

serine protease inhibitor contains at least one intra-chain cysteine-cysteine disulfide bond selected from the cysteine-cysteine paired groups consisting of CYS11-CYS61, CYS20-CYS44, CYS36-CYS57, CYS106-CYS156, CYS115-CYS139, and CYS131-CYS152, wherein the cysteine residues are numbered according to the amino acid sequence of native human placental bikunin.